Diffuse Large B-Cell Lymphoma of the Uterine Cervix: A Rare Case and Review of Literature

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Summary

Extra nodal Non Hodgkin`s Lymphoma of the genital tract accounts for less than 1% of all the NHLs. Most commonly involves the ovary followed by cervix, vulva and vagina in descending order. Most of the genital tract lymphomas present in early stage and Diffuse Large B Cell Lymphoma (DLBCL) is the most common histology. Indolent lymphomas can also present with primary genital tract involvement. Diagnosis is confirmed by histopathology and immuno-histochemistry. PET is used for staging and assessment of bone marrow. There are no standard treatment guidelines for this entity and management is based grossly on the principles of management of nodal lymphomas. Here we present a case of DLBCL of uterine cervix presenting with obstructive uropathy, who underwent haemodialysis and per cutaneous nephrostomy followed by one cycle of chemo therapy and succumbed to severe febrile neutropenia.

Keywords: Diffuse large B Cell Lymphoma, Extranodal, Genital tract, Uterine cervix

Introduction

Extra nodal Non Hodgkin's lymphoma (NHL) of the genital tract accounts for less than 1% of all NHLs.[1] Isolated gynaecological NHL involves the ovary in 59% of the cases, uterine cervix in 15.5%, vulva in 7.5% and vagina in 6%.[2] Most common histology is Diffuse Large B cell lymphoma (DLBCL)-37%, followed by follicular lymphoma (FL). Median age of diagnosis is 46 years (range 20-85 years). Majority of these tumours present in early stage i.e. Stage I-69.2%, stage II-22.7%, stage III and IV-8.1%. Therapeutic approach to these tumours is not standardised but based on general principles of treatment of NHL.[3] Here we present a rare case report of primary diffuse large B cell lymphoma of the uterine cervix.

Case Report

A 68-year-old, post-menopausal female with no known co-morbidities came to our institute with a history of post menopausal bleeding since 15 days. Her clinical pelvic examination revealed transversely enlarged, globular uterine cervix with an open os with a mass seemingly within the endo-cervix. Examination of the para-metrium revealed involvement bilaterally till the pelvic wall making it FIGO stage IIIB. A punch biopsy of the endo-cervical mass was performed which was morphologically suggestive of poorly differentiated carcinoma. Immuno-histochemistry (IHC) revealed presence of Lymphocyte common antigen (LCA), PAX8, PAX5, CD20, BCL 6 and MUM1 and negative for AE1 and BCL2. MIB1 was 70-80%.

Diagnosis of DLBCL was established. Viral markers for HIV (Human immunodeficiency virus), HbsAg (Hepatitis B surface antigen), HCV (Hepatitis C virus) were negative. She had Haemoglobin of 8.2, liver function was normal. Her serum creatinine level on presentation was 3.39 which raised to 9.64 within a week's time. She had to undergo a couple of sessions of haemo-dialysis followed by placement of percutaneous nephrostomy in view of moderate hydro-uretero-nephrosis on the left side. Post procedurally the creatinine level was down trending and she could undergo evaluation with whole body Positron emission tomography (PET) alone without computed tomography (CT) which revealed a large conglomerated mass lesion in lower abdomen and pelvic region involving mesentery, encasing bowel loops in mid line and left iliac fossa, uterus, cervix upper vagina, infiltrating the posterior wall of bladder and encasing both ureters causing proximal hydro-uretero-nephrosis. Size of the lesion was 10.3x9.3x1.2 cm with SUV max of 31.2. Few para rectal nodes were present of about 1x1 cm with SUV max of 5.6. There was a conglomerated lymph nodal mass involving para-aortic, left common iliac and left external iliac region of size 4.7x3.2 cm with SUV max 32.8. In the mediastinum a left hilar node of 1.3x0.7 cm was present with SUV max of 6.4. Multiple bilateral lung infiltrates were present, largest measuring 1.7x1.7 cm with SUV max of 12.6. She was Ann Arbor stage IV with IPI (International Prognostic Index) of 5 falling in poor risk category. She was started on chemo-immunotherapy as her cardiac reserve was normal. She was given rituximab, cyclophosphamide, adriamycin, vincristine and prednisolone (R-miniCHOP with 50% dose reduced cyclophosphamide, adriamycin, vincristine). She developed grade IV febrile neutropenia post first cycle of chemotherapy and succumbed to pneumonitis.

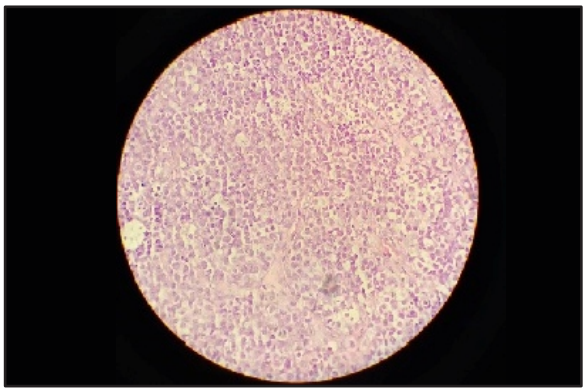

Figure 1: Heamatoxylin and eosin staining

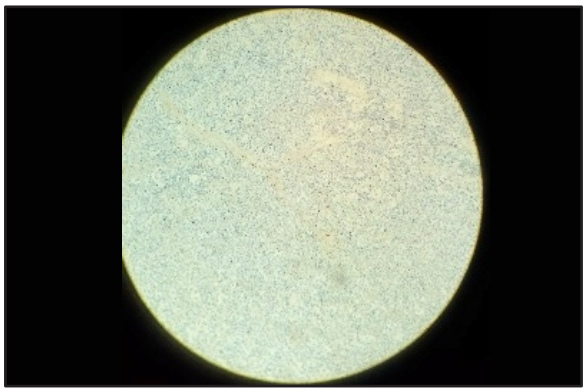

Figure 2: AE-1 IHC marker negative

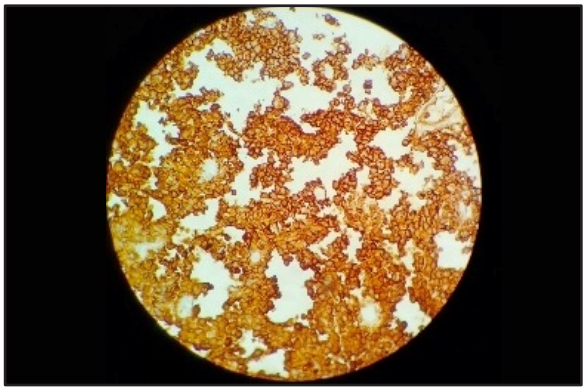

Figure 3: CD20 positivity on IHC

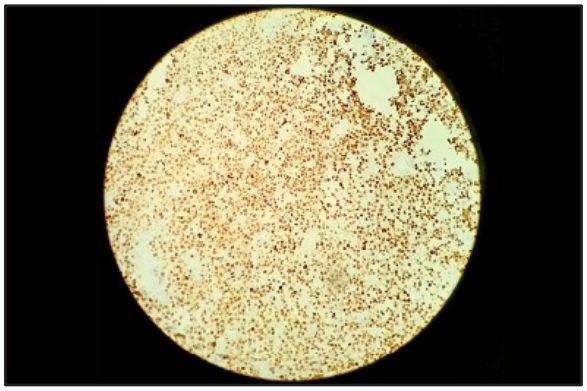

Figure 4: MIB1 High (70-80%)

Discussion

The question whether this is a primary lymphoma of the uterine cervix or secondary extra nodal involvement remains. Extra nodal involvement is seen in one in every four cases of Non Hodgkin's Lymphoma. Female genital tract as a site of extra nodal involvement is seen in 1-1.5% of the cases.[4] Primary Non Hodgkin's lymphoma of the uterine cervix accounts for 0.12% of all cases.[5] In view of major bulk of the disease and metabolic activity residing within the cervix and para aortic nodes and the presenting symptom and sub centimetric hilar nodes, an assumption of primary from the cervix was made. In either case this is a rare presentation and hence has been reported. Predominant symptoms of genital tract extra-nodal NHL are dysfunctional uterine bleeding, cervical or pelvic mass and pain in descending order. Early stages can present without symptoms, 'B' symptoms are rare compared to nodal DLBCL.[3] Our patient presented with bleeding per vaginum and obstructive uropathy akin to squamous cell carcinoma of the cervix. For the lymphoma of uterine cervix, lack of involvement of mucosa, sparing of stroma and junctional zone are characteristic.[6] Uterine cervix lymphomas should be distinguished from sarcoma, poorly differentiated carcinoma, neuroendocrine tumours, malignant melanoma, malignant mixed Mullerian tumour, extra-osseous Ewing's and chronic cervicitis.[7] From the reports in literature, therapeutic approach ranged from surgery with adjuvant radiotherapy for localised disease to adjuvant chemotherapy for advanced disease to systemic chemotherapy alone. Over the last few years, immuno-chemotherapy combination regimens have established efficacy. The therapeutic value of surgery is limited besides providing histological diagnosis.[3] Few reports state that for localised NHL with aggressive histology offering radiotherapy post chemotherapy does not seem to offer any benefit in progression free or overall survival.[8] Few reports quote that many patients achieve prolonged progression free survival with combination of chemotherapy and involved field radiotherapy.[7] Cure rates are good in patients with limited disease (5-year PFS of 80-85%) where- as approximately a 50% 5-year PFS of can be observed in patients with advanced disease. The treatment regimen of choice is CHOP chemotherapy combined with Rituximab, a mono-clonal anti-CD20 antibody.[9] Central nervous system prophylaxis with intrathecal methotrexate has been used by few in literature.[7] As in nodal DLBCL role of autologous bone marrow transplant has no role in first remission but indicated for relapsed, refractory disease.[9]

Conclusion

Primary DLBCL of the uterine cervix is a rare disease. There are no standard guidelines for the management. Majority of reports in literature used PET scan for staging, chemo-immunotherapy as primary treatment, involved field radiotherapy and CNS prophylaxis have been used in few reports. More case reports or series with long term follow up may shed light regarding standard management of this entity.

Acknowledgements

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